AMENDMENTS TO THE SPECIFICATION:

Please amend the specification as follows:

After the Figures, insert pages 1 through 25 of the Sequence Listing submitted herewith.

Please amend the paragraph on page 1, after the Title which starts with "This application" as follows:

This application is a continuation of United States Application Serial No. 09/121,457 filed July 23, 1998, now U.S. Patent No. 6,692,919, which is a continuation-in-part of co-pending United States Application Serial No. 08/899,232 filed July 23, 1997, now U.S. Patent No. 6,436,650, which are incorporated by reference herein in their entirety.

Please amend the paragraph on page 7, line 15 which starts with "Insight" as follows:

Insight into the developmental role and the general nature of Notch signaling has emerged from studies with truncated, constitutively activated forms of Notch in several species. These recombinantly engineered Notch forms, which lack extracellular ligand-binding domains, resemble the naturally occurring oncogenic variants of mammalian Notch proteins and are constitutively activated using phenotypic criteria (Greenwald, 1994, Curr. Opin. Genet. Dev. 4:556; Fortini et al., 1993, Nature 365:555-557; Coffman et al., 1993, Cell 73:659-671; Struhl et al., 1993, Cell 69:1073; Rebay et al., 1993, Cell 74:319-329 ~~Genes Dev. 7:1949~~; Kopan et al., 1994, Development 120:2385; Roehl et al., 1993, Nature 364:632).

Please amend the paragraph on page 7, line 27 which starts with "Ubiquitous" as follows:

- Ubiquitous expression of activated Notch in the Drosophila embryo suppresses neuroblast segregation without impairing epidermal differentiation (Struhl et al., 1993, Cell 69:331; Rebay et al., 1993, Cell 74:319-329 ~~Genes Dev. 7:1949~~).

Please amend the paragraph on page 13, line 1 which starts with "Figure 2" as follows:

Figures 2A-2D depict ~~Figure 2 is~~ a Notch homolog sequence comparison. The human Notch2 (humN2) (SEQ ID NO:1), human Notch1 (humN1) (SEQ ID NO:2), *Xenopus* Notch/Xotch (XenN) (SEQ ID NO:3), and *Drosophila* Notch (DrosN) (SEQ ID NO:4) protein sequences are aligned, with names indicated to the left and numbering to the right (Wharton et al., 1985, Cell 43:567-581; Coffman et al., 1990, Science 249:1438-1441; Ellisen et al., 1991, Cell 66:649-661; Stifani et al., 1992, Nature Genetics 2:119-127). Major Notch protein motifs are enclosed in boxes. Starting from the N-terminal, the boxed regions indicate: EGF repeats,

Lin-12/Notch (LN) repeats, transmembrane domain (TM), Ankyrin repeats, and PEST-containing region. Also indicated are the putative CcN motif components (Stifani et al., 1992, Nature Genetics 2:119-127) nuclear localization signal (NLS, BNTS) and putative CKII and cdc2 phosphorylation sites. The calculated signal cleavage site is indicated with an arrow.

Please amend the paragraph on page 23, line 25 which starts with "Various procedures" as follows:

Various procedures known in the art may be used for the production of polyclonal antibodies to a Notch protein or peptide. In a particular embodiment, rabbit polyclonal antibodies to an epitope of the human Notch proteins depicted in Figures 2A-2D ~~Figure 2~~, or a subsequence thereof, can be obtained. For the production of antibody, various host animals can be immunized by injection with the native Notch protein, or a synthetic version, or fragment thereof, including but not limited to rabbits, mice, rats, etc. Various adjuvants may be used to increase the immunological response, depending on the host species, and including but not limited to Freund's (complete and incomplete), mineral gels such as aluminum hydroxide, surface active substances such as lysolecithin, pluronic polyols, polyanions, peptides, oil emulsions, keyhole limpet hemocyanins, dinitrophenol, and potentially useful human adjuvants such as BCG (bacille Calmette-Guerin) and corynebacterium parvum.

Please amend the paragraph on page 47, line 2 which starts with "The full-length" as follows:

The full-length cDNA encoding the human Notch2 protein is 7.8 kb in length, and the predicted protein product is 2471 amino acids long. This protein has all of the expected domains of Notch family proteins and is 92% identical to the rat Notch2 amino acid sequence overall. An amino acid alignment of human Notch2 (SEQ ID NO:1) with human Notch1 (SEQ ID NO:2), *Xenopus* Notch (Xotch) (SEQ ID NO:3) and *Drosophila* Notch (SEQ ID NO:4) is shown in Figures 2A-2D ~~Figure 2~~.

Please amend the paragraph on page 51, line 14 which starts with "In the aforementioned" as follows:

In the aforementioned pulse labeling experiments (Figures 6A-6B) ~~(Figure 6)~~, the accumulation of the N^{TM} fragment is closely paralleled by the accumulation of a larger fragment that is approximately 180 kD in molecular weight. This larger fragment is co-immunoprecipitated by the antibody PGHN, which recognizes an intracellular epitope of human

Notch2. However, blotting of the same immunoprecipitate by western blot, using antibody bhN6D, also raised against an intracellular epitope, detects only the N^{TM} fragment.

Please amend the paragraph on page 51, line 24 which starts with "A single cleavage" as follows:

A single cleavage of the Notch protein that produces a 110 kD fragment would also generate a second fragment of approximately 180 kD. It was therefore presumed that the N^{EC} fragment, which accumulates with kinetics indistinguishable from those of N^{TM}, corresponds to the cleaved extracellular domain of the Notch2 protein that remains attached to the N^{TM} polypeptide by a SDS and/or DTT sensitive linkage. Antibodies recognizing extracellular epitopes were not possessed by us for western blot analysis. However, the relatedness of these fragments is also supported by the fact that the appearance of N^{EC} is not inhibited by monensin or chloraquinone (data not shown) but is inhibited by Brefeldin A and a 19°C block (Figure 6A) ~~(Figure 6)~~. Additional supporting evidence comes from pulse labeling experiments done with a cysteine rather than a methionine label. Labeling with cysteine shows that the N^{EC} band incorporates nearly an order of magnitude more label than the N^{TM} band, consistent with the hypothesis that it carries most of the Notch extracellular domain (data not shown).

Please amend the paragraph on page 54, line 19 which starts with "The biological" as follows:

The biological significance of the heterodimeric Notch form would be questionable if it could not bind ligands. Physical interaction between the extracellular domains of Notch and Delta have been demonstrated with the help of aggregation assays involving Delta and Notch expressing cells. If the heterodimeric form interacts with Delta after aggregation then the 110 kd N^{TM} fragment should co-immunoprecipitate using Delta antibodies. It was found that after aggregation, Delta antibodies are capable of efficiently immunoprecipitating the N^{TM} fragment demonstrating that the heterodimeric form can bind Delta (Figure 8). As expected, if the aggregation is disrupted by depleting calcium from the medium by EGTA ~~(Fehon et al., 1993, Cell 61:523-534). Delta~~ (Fehon et al., 1993, Cell 61:523-534), Delta antibodies fail to efficiently precipitate N^{TM} (data not shown).